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10/561,864	01/28/2008	Kyung-Lim Lee	3450-0101	5528

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EXAMINER

SEHARASEYON, JEGATHEESAN

ART UNIT	PAPER NUMBER
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1646

NOTIFICATION DATE	DELIVERY MODE
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08/05/2010

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

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PTO-PAT-Email@rfem.com

Office Action Summary	Application No. 10/561,864	Applicant(s) LEE ET AL.	
	Examiner JEGATHEESAN SEHARASEYON	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 May 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) 1-6 and 10-16 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 7-9 and 17-20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. This Office Action in response to Applicant's amendments and remarks filed 5/7/10. Claims 1-20 are pending. Claims 7-9 have been amended. Claims 17-20 are newly added drawn to the instant invention. Claims 1-6 and 10-16 were previously withdrawn. Therefore, claims 7-9 and 17-20 are pending and examined.

2. Any objection or rejection of record, which is not expressly repeated in this action, has been overcome by Applicant's response and withdrawn.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

3a. The rejection of claims 7-9, 19 and 20 under 35 U.S.C. 102(e) as being over Bartel by (U. S. Patent No. 2002/0177692) is maintained for reasons set forth in the Office Action dated 1/7/10.

Applicant is arguing that the identified active compound cannot be used as an antihypertensive drug, but that the active compound identified in accordance with Bartel can be administered in combination with a hypertensive drug.

Applicant also asserts that Bartel reference teaches that BCL-XL and TCTP may

Art Unit: 1646

play a role in apoptosis [p. 0015]. Further, Applicant asserts that the laundry list of diseases disclosed in paragraph 0020 does not disclose hypertension. Thus, Applicant claims that Bartle clearly fails to recognize that compound identified using BCL-XL and TCTP may be used to treat hypertension. In addition, Applicant also argues that the reference does not teach if the compound identified inhibits the function of TCTP function.

Applicant's arguments have been fully considered but are not found to be persuasive. With respect to Applicant's assertion that the reference does not teach an antihypertensive drug but an active compound that synergistically treats or prevents hypertension with a hypertensive drug, for the compounds disclosed to have synergistic effect both these compounds need to have antihypertensive effect. Thus, absent evidence to the contrary it is expected that the active compound identified will contain an antihypertensive effect which will produce a synergistic effect with a hypertension drug. Contrary to Applicant's assertion that the reference only teaches the modulation of Apoptosis, the reference does teach the modulation of TCTP to treat other diseases [0015]. While, paragraph 20, does not disclose hypertension paragraph 293 does contemplate the treatment of hypertension. Further, the inhibition of the protein synthesis and/or interaction is taught on paragraph [0194 and 0216]. Therefore, the rejection of record is maintained.

3b. Claims 7-9 and 17-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Fujise et al. (U.S. Patent No. 7,691,567).

Claims are drawn to method for screening antihypertensive drugs.

Fujise et al. discloses methods for screening modulators of Fortilin polypeptide (col. 5, lines 16-20). Fortilin polypeptide is also known as Translationally Controlled Tumor Protein (TCTP) of SEQ ID NO: 2 (col. 5, lines 10-15 and col. 10, lines 36-40), which is identical to the instant invention. The nucleotide encoding the polypeptide is disclosed in SEQ ID NO: 1 (col. 5, line 15). The screening of the test compounds using high throughput screening (col. 67, lines 4-8), in vitro assays (col. 66, lines 56-65) and other methods (see cols. 64-65). The reference discloses that an inhibitor according to the reference may be one which exerts its inhibitory or activating effect upstream, downstream or directly on Fortilin. Further, the reference teaches that the effect of the inhibition or activation by the compounds identified results in alteration in Fortilin activity as compared to that observed in the absence of the added candidate substance (col. 66, lines 40-47). Fujise et al. discloses that compounds identified can be used in the treatment of hypertension (col. 83, lines 50-63). Therefore, claims 7-9 and 17-20 are anticipated by Fujise et al.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4a. Claim 18 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide expressed from SEQ ID NO: 1 does not reasonably provide enablement for all active fragment of TCTP

Art Unit: 1646

protein, a gene sequence having one or more disruption, deletion, insertion, point mutation, substitution, nonsense, missense, polymorphism or rearrangement mutations in a base sequence of SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is “undue” include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Claim 18 is drawn to a composition comprising surfactant proteins used for the treatment gastrointestinal infections in mammals. Although, claim 18 provides for the use of various variants of TCTP, there is no disclosure of the structure of the various variants/derivatives disclosed in the specification. The specification discloses TCTP encoded by SEQ ID NO: 1 in page 4. Although the specification describes mutations contemplated, the specification does not teach

Art Unit: 1646

how to generate various active fragments, derivatives and mutations contemplated in the instant invention. There are no examples of other than SEQ ID NO: 1 and 2. In addition, claim 18 does not recite the structure required to treat gastrointestinal infections in mammals.

The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants growth promotion or treating an inflammatory pathology or other functional attributes of the instant polypeptide. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, *Biochemistry* 29:8509-8517; Ngo et al., 1994, *The Protein Folding Problem and Tertiary Structure Prediction*, pp. 492-495). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although the

Art Unit: 1646

specification outlines art-recognized procedures for producing and screening for active muteins, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. Therefore, predicting which polypeptide(s), if any, would retain the functions of the protein is well outside the realm of routine experimentation. Thus, an undue amount of experimentation would be required to generate the changes/modifications contemplated and yet retain the function of the proteins claimed.

A large quantity of experimentation would have been necessary for the skilled artisan to generate all the active mutations and active fragments of TCTP encoding sequences etc recited in the claims and possibly screen the same for a useful activity. The specification fails to provide sufficient direction/guidance regarding which structural features are required in order to provide the activity to the fragments and derivatives etc. There are no working examples directed to all the compounds contemplated in the instant invention to treat gastrointestinal infections. The nature of the invention is complex, involving the generation of compositions comprising surfactant –associated proteins that are capable of treating gastrointestinal infection in mammals. In fact claim 18 provides no

Art Unit: 1646

structural requirement to confer the functional activity. The state of the prior art establishes the unpredictability of the effects of variants. In addition, the breadth of the claims is large, failing to recite any structural or functional limitations.

Applicant has not taught how one of skilled in the art would use the full scope of compounds encompassed by the invention of claim 18. The specification as filed does not sufficiently teach one of skilled in the art how to make and/or use the full scope of the claimed sequences. The amount of experimentation required to make and/or use the full scope of the claimed sequences would require trial and error experimentation to determine the functional sequences.

Given the breadth of claim 18 in light of the unpredictability of the art as determined by the lack of working examples and as shown by the prior art of record, the level of skill of the artisan, and the lack of guidance provided in the instant specification, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention in its full scope.

4b. Claim 18 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a written description rejection.

The specification discloses TCTP encoded by SEQ ID NO: 1. This disclosure meets the written description provisions of 35 USC 112, first paragraph. However, the instant specification fails to provide adequate written

Art Unit: 1646

description to the various active fragments of TCTP containing various mutations of polypeptide contemplated by the instant invention. Since the instant claims are drawn to composition comprising various TCTP polypeptide for the screening of antihypertensive drugs, they lack written description. Although, compositions comprising various variants of the TCTP are claimed there is no disclosure of the structure to accomplish the screening of antihypertensive drugs. The claims as written, however, encompass various compounds which were not originally contemplated and fail to meet the written description provision of 35 USC 112, first paragraph because the written description is not commensurate in scope with the recitation of claim 18. The specification does not provide written support for the genus encompassed by the instant claims.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, there is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. The specification does not provide written description to support the genus encompassed by the instant claims.

Art Unit: 1646

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the ‘written description’ inquiry, *whatever is now claimed*.” (See page 1117.) The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed” (See *Vas-Cath* at page 1116).

With the exception of TCTP encoded by SEQ ID NO: 1 (polypeptide of SEQ ID NO: 2), the skilled artisan cannot envision all the detailed chemical structures of the compounds regardless of the complexity or simplicity of the method of isolation.

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The polypeptide itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes v. Baird*, claims directed to mammalian FGF’s were found unpatentable due to lack of written description for the broad class.

Therefore, only the isolated polypeptide of SEQ ID NO: 2 and polynucleotide of SEQ ID NO: 1 for screening an antihypertensive drug but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed mutants are not representative of the genus because the genus is highly variant. As a result, it does not appear that the inventors were in possession of various compositions set forth in claim 18.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.) Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 “Written

Art Unit: 1646

Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

Conclusion

5. No claims are allowed.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JEGATHEESAN SEHARASEYON whose telephone number is (571)272-0892. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol, Ph. D can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jegatheesan Seharaseyon/
Examiner, Art Unit 1646

JS
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